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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,979		William Melvin	1012-103US	2841

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QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.
P O BOX 458
ALAMEDA, CA 94501

EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 09/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/936,979	MELVIN ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *19-25* is/are withdrawn from consideration.

5)☒ Claim(s) *2-9* is/are allowed.

6)☒ Claim(s) *10-18* is/are rejected.

7)☒ Claim(s) *1* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

The Election filed on June 19, 2006 in response to the Restriction Requirement of 3/17/2006 has been entered. Applicant's election of Group I, claims 1-14, as specifically drawn to the special technical feature of an antibody and a method of producing the antibody, wherein the antibody, wherein the antibody binds to a peptide consisting of an amino acid of VNQWSVNHDPVKWPN with traverse has been acknowledged.

The traversal is on the grounds that an inventive linkage exists between the alternate sequences of the claims, it would not be a serious burden on the Office to search and prosecute the present application based on the proposed groupings and that the restriction is improper according to the rule of In re Harnisch. For example, Applicants assert that the sequences are continuation of each other in region of the CYP1B1 protein sequence identified as substantially unique and available for antibody interactions. Specifically, Applicants submit that VNQWSVNHDPVKWPN represents amino acids 437 to 451 of the CYP1B1 protein and PENFDPARFLDKKGL represents amino acids 437 to 451 of the protein.

These arguments have been carefully considered and have been found to be persuasive. As such, Group II will be rejoined with Group I for prosecution of the merits.

Therefore, the restriction requirement is deemed to be proper and is made FINAL.

Claims 1-25 are currently pending

Claims 19-25 are withdrawn from consideration as being drawn to a non-elected invention.

Claims 1-18 are currently under consideration.

Priority

If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 371, a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

If the instant application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the

application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Information Disclosure Statement

The Information Disclosure Statement filed on 3/14/2002 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. A signed copy of the IDS is attached hereto.

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

The disclosure is objected to because of the following informalities: The specification is objected to on page 18 and 26 for improper disclosure of amino acid sequences without a respective sequence identifier, i.e. a SEQ ID NOs:. Hence, the disclosure fails to comply with the requirements of 37 CFR 1.821 through 1.825. In the absence of a sequence identifier for each sequence, Applicant must provide a computer readable form (CRF) copy of the sequence listing, an initial or substitute paper copy of the sequence listing, as well as any amendment directing its entry into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 CFR 1.821(e-f) or 1.825(b) or 1.825(d).

Appropriate correction is required.

Claim Objections

Claims 1 and 10 are objected to because of the following informalities: Claims 1 and 10 are objected to for improper disclosure of amino acid sequences without a respective sequence identifier, i.e. a SEQ ID NOs:. Hence, the claims fail to comply with the requirements of 37 CFR 1.821 through 1.825. In the absence of a sequence identifier for each sequence, Applicant must

provide a computer readable form (CRF) copy of the sequence listing, an initial or substitute paper copy of the sequence listing, as well as any amendment directing its entry into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 CFR 1.821(e-f) or 1.825(b) or 1.825(d).

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 10-18, as written, do not sufficiently distinguish over antibodies as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified" as taught by page 15, line 2 of the specification. See MPEP 2105.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10-12 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Pottenger et al. (Arch. Biochem. Biophys. 1991; 286: 488-497) as evidenced by Accession Number NP_034124.

Pottenger et al. teach polyclonal antibodies raised to a protein referred to as P450-EF isolted from mouse embryo fibroblast derived C3H/10T1/2 CL8 cells (abstract and page 490, 1st column, *Immunological Studies*). Thus, while Pottenger et al. do not specifically teach that the protein referred to as P450-EF is synonymous with P450 CYP1B1, the claimed limitation does not appear to result

in a manipulative difference when compared to the prior art because Accession Number NP_034124 (see below) refers to P450-EF in the Pottenger et al. reference as P450 CYP1B1. Moreover, although Pottenger et al. does not specifically teach that the polyclonal antibody to P450-EF recognizes an epitope in the cytochrome P450 CYP1B1 protein included within the amino acid sequence VNQWSVNHDPVKWPN or PExFDPARFLDKDGy, wherein X is D or N and y is L or F, the claims are drawn to the product *per se* and inherently, such a polyclonal antibody would "specifically bind" to that epitope, in addition to other ones found in the p450 protein. Thus, the claimed antibody appears to be the same as the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989). Lastly, even though Pottenger et al. does not explicitly teach an antibody for use in a method of medical treatment, the intended use of the compound must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. A composition is a composition irrespective of what its intended use is. See In re Tuominen, 213 USPQ 89 (CCPA 1982).

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REFERENCE   26 (residues 1 to 543)
  AUTHORS   Pottenger,L.H., Christou,M. and Jefcoate,C.R.
  TITLE     Purification and immunological characterization of a novel
            cytochrome P450 from C3H/10T1/2 cells
  JOURNAL   Arch. Biochem. Biophys. 286 (2), 488-497 (1991)
   PUBMED   1910294
COMMENT     PROVISIONAL REFSEQ: This record has not yet been subject to final
            NCBI review. The reference sequence was derived from U03283.1.
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                     /coded_by="NM_009994.1:357..1988"
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                     /go_function="heme binding; iron ion binding; metal ion
                     binding; monooxygenase activity; oxidoreductase activity;
                     unspecific monooxygenase activity"
                     /go_process="electron transport"
                     /db_xref="GeneID:13078"
                     /db_xref="MGI:88590"
ORIGIN
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       61 gnaaavgqas hlyfarlarr ygdvfqirlg scpvvvlnge saihqalvqq gsifadrppf
      121 asfrvvsggr slafghyseh wktqrrsays tmrafstrhp rsrgllegha laearelvav
      181 lvrrcaggaf ldptqpviva vanvmsavcf gcrynhddae flellshnee fgrtvgagsl
      241 vdvlpwlqlf pnpvrttfrk feqlnrnfsn fvldkflrhr eslvpgaapr dmtdafilsa
      301 ekkasgapgd dssgldledv patitdifga sqdtlstall wllilftryp dvqarvqael
      361 dqvvgrdrlp cmsdqpnlpy vmaflyesmr fssflpvtip hattantfvl gyyipkntvv
      421 fvnqwsvnhd pakwpnpedf dparfldkdg finkalassv mifsvgkrrc igeelskmll
      481 flfisilahq cnfkanqnes snmsfsyglt ikpksfrihv slresmelld navkklqtee
      541 gck
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Claims 10-13 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Melvin et al. (WO 97/12246, 1997, IDS).

Melvin et al. teach monoclonal and polyclonal antibodies that bind to p450 CYP1B1 protein. Specifically, the WO document teaches that antibodies that react with human p450 CYP1B1 protein can be generated by using a preparation of non-human CYP1B1 protein, e.g., murine CYP1B1 (beginning on page 8, *Preparation of antibodies*). Thus, while Melvin et al. do not explicitly teach that the polyclonal antibodies recognize an epitope in the cytochrome P450 CYP1B1 protein included within the amino acid sequence VNQWSVNHDPVKWPN or PExFDPARFLDKDGy, wherein X is D or N and y is L or F, the claimed limitation does not appear to result in a manipulative difference between the prior art's polyclonal antibodies because the specification teaches (page 26, lines 4-17) that amino acid residues FDPARFLDKDG are identical in three p450's, rat CYP1B1, mouse CYP1B1 and human CYP1B1. Thus, a polyclonal antibody generated using murine p450

would "specifically bind" to that epitope, in addition to other ones found in the p450 protein. Thus, the claimed antibody appears to be the same as the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989). Lastly, even though Melvin et al. does not explicitly teach an antibody for use in a method of medical treatment, the intended use of the compound must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. A composition is a composition irrespective of what its intended use is. See In re Tuominen, 213 USPQ 89 (CCPA 1982).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Melvin et al. (WO 97/12246, 1997, IDS) in view of Chiocca et al. (US 5,688,773, 1997).

Melvin et al. teach, as applied to claims 10-13 and 18 above, monoclonal and polyclonal antibodies that bind to p450 CYP1B1 protein. Specifically, the WO document teaches that antibodies that react with human p450 CYP1B1 protein can be generated by using a preparation of non-human CYP1B1 protein, e.g., murine CYP1B1 (beginning on page 8, *Preparation of antibodies*). Moreover, the Wo document teaches that the antibodies are used in tumor diagnosis by detecting CYP1B1 (page 7, 2nd full paragraph).

Melvin et al. do not explicitly teach that the antibody is labeled.

Chiocca et al. teach that the expression of nonhuman or unique surface antigens in neoplastic cells can be located on such neoplastic cells by subsequence biding with labeled antibodies (column 13, lines 24-26).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to label an antibody as taught by Melvin et al. in view of Chiocca et al. One would have been motivated to do so because Chiocca et al. teach labeled antibodies are used to identity the expression patterns of unique surface antigens present on neoplastic cells. As such, labeling antibodies for purposes of determining expression patterns of a surface antigen on neoplastic cells is well known in the art. Thus, one of ordinary skill in the art would have a reasonable expectation that by labeling an antibody taught by Melvin et al., one would achieve a method of measuring the expression patterns of CYP1B1 on neoplastic cells for the purposes of diagnosis.

Conclusion

In the instant case, Melvin et al. (WO 97/12246, 1997, IDS), considered to be the closest prior art, teaches monoclonal and polyclonal antibodies that bind to p450 CYP1B1 protein, as well as a method of preparing said antibodies. However, Melvin et al. does not teach or suggest a method of making an antibody that specifically binds to cytochrome p450 CYP1B1 comprising raising antibodies using a peptide consisting of an amino acid sequence VNQWSVNHDPVKWPN or PExFDPARFLDKDGy, wherein X is D or N and y is L or F as recited in pending claims 1-9 and 15. Nor do Melvin et al. explicitly teach or suggest using the antibody in vivo such that one

would be motivated to generate a humanized antibody as recited in pending claim 14. As such, claims 1-9 and 14-15 appear to be free of the prior art. Claims 1-9 appear to be in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brandon J Fetterolf, PhD
Patent Examiner
Art Unit 1642

BF

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER